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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/987,482	11/14/2001	Pooman Bhandari	056859-0134	7065

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EXAMINER	
PARAS JR, PETER	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant( )
	09/987,482	BHANDARI ET AL.
	Examiner	Art Unit
	Peter Paras, Jr.	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *2,3,5-9,11,13-18 and 20-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,10,12 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 November 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *0603* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The preliminary amendment received on 4/3/02 has been entered. Claims 4-9, 13, 15, 17, 18, 22-27, 31, 33, 35, and 36 have been amended. Claims 1-36 are pending.

Election/Restrictions

Applicant's election with traverse of Group I in Paper No. 9 is acknowledged. The traversal is on the ground(s) that the Examiner has not shown that a serious burden would be required to examine all the claims. This is not found persuasive because each of the Inventions requires a separate search status. In particular, it is maintained that the products of Groups I, II, and III are distinct each from the other because the products of the groups are transgenic *Drosophila* having different chemical structures each from the other. Since the products of Groups I-III are different structurally, they are used separately and restriction between such is proper. Accordingly, since the products of Groups I-III are different, a separate search is required for each.

It is maintained that the methods of Groups IV-IX are distinct, comprising different methodologies that use different products and require different technical considerations each from the other. For example, the method of Group IV requires cross-breeding different *Drosophila* strains; the method of Group V requires screening for differentially expressed genes using differential display-RT PCR or microarray techniques; the method of Group VI requires identifying differentially expressed proteins using proteomics techniques; the method of Group VII is directed to studying Wnt/Wg signaling by crossing transgenic *Drosophila* with GAL4 drivers; the method of Group VIII

is directed to identifying a human APC pathway using drugs that are anti-inflammatory, analgesics, antipyretics, or antineoplastics; and the method of Group IX is directed to a method of screening for compounds that have anti-cancer activity. Accordingly, for the reasons of record, it is maintained that each of the methods of Groups IV-IX is different from the other and separately searched.

It is further maintained that Inventions I-III and IV-IX are properly restricted. Inventions I-III and IV-IX are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). It is maintained that the process for using the product as claimed can be practiced with other materially different products and the products as claimed can be used in materially different processes. For example, the claimed methods of Groups IV-IX can be practiced with different transgenic *Drosophila* while the claimed transgenic *Drosophila* of Groups I-III can be used in different methods from the methods of Groups IV-IX; the transgenic Drosophila of Groups I-III, for example, can be used to produce a protein. Accordingly, for the reasons of record, it is maintained that the inventions of Groups I-IX are separately searched.

Therefore it is maintained that all the inventions are distinct each from the other for the reasons given above. The requirement is still deemed proper and is therefore made FINAL.

Please note that after a final requirement for restriction, the Applicants, in addition to making any response due on the remainder of the action, may petition the Commissioner to review the requirement. Petition may be deferred until after final action on or allowance of claims to the invention elected, but must be filed not later than appeal. A petition will not be considered if reconsideration of the requirement was not requested. (See § 1.181.).

Claims 2-3, 5-9, 11, 13-18, and 20-36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

Drawings

New corrected drawings are required in this application because Figures 1-5 are photocopies and are illegible. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded

hyperlink and/or other form of browser-executable code. See MPEP § 608.01. For example see pages 6, 34, 35 of the specification.

Claim Objections

Claim 19 objected to under 37 CFR 1.75 as being a substantial duplicate of claim1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim 10 is objected to because of the following informalities: the term "method" should not be capitalized. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1 and 19 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966). See part (d) of claims 1 and 19.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4, 10, 12, and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a transgenic *Drosophila* whose genome comprises the full-length human colon cancer gene Adenomatous Polyposis Coli (hAPC) gene having SEQ ID NO: 1 wherein said transgenic *Drosophila* exhibits developmental abnormalities. The claims are further directed to methods of using the same transgenic *Drosophila* to screen for compounds that may inhibit or enhance the phenotypes exhibited said transgenic *Drosophila*.

The nucleotide sequences of the human colon cancer gene APC encompassed within the genus have not been disclosed. The claims as written embrace the full-length human colon cancer gene APC having SEQ ID NO: 1, which can be properly interpreted to mean that the nucleotide sequence of the gene is set forth in SEQ ID NO: 1. However, SEQ ID NO: 1 as set forth in the sequence listing of the instant application comprises an amino acid sequence. As such it does not appear that the instant specification has disclosed the nucleotide sequence of the APC gene. Moreover, the

term gene can be interpreted to read on cDNA or genomic sequences of the APC gene. If the term gene is intended to embrace the APC genomic sequence, the art recognized attributes of the term gene have not been described by the instant specification. For example, the promoter region, intron/exon boundaries, and 5' and 3' ends of the APC genomic gene sequence have not been described by the instant specification. If the term gene is intended to embrace the APC cDNA sequence, as previously stated the instant specification has not described any nucleotide sequence of the APC gene.

Based upon the prior art there is expected to be variation among the species of DNAs, which encode hAPC, because the sequence of hAPC DNAs would be expected to vary among individuals. The specification discloses the amino acid sequence of human APC (SEQ ID NO: 1) but does not disclose any DNA sequence encoding hAPC. There is no evidence on the record of a relationship between the structure of any hAPC DNA and the hAPC gene sequence embraced by the claims that would provide any reliable information about the structure of APC DNA sequences within the genus. There is no evidence on the record that the hAPC gene embraced by the claims had a known structural relationship to any other hAPC DNA sequences; the specification discloses only an hAPC amino acid sequence (SEQ ID NO: 1); the art indicated that there is variation between hAPC DNA sequences. In view of the above considerations one of skill in the art would not recognize that applicant was in possession of the necessary common features or attributes possessed by member of the genus of APC genes, because an hAPC amino acid sequence is not representative of the claimed genus. Consequently, since Applicant was in possession of only the hAPC amino acid

sequence and since the art recognized variation among the species of the genus of hAPC DNA sequence, the hAPC amino acid was not representative of the claimed genus of hAPC genes. Therefore, Applicant was not in possession of the genus of hAPC genes as encompassed by the claims. University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that to fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention."

Claims 1, 4, 10, 12 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transgenic *Drosophila* whose genome comprises a nucleotide sequence encoding full-length human Adenomatous Polyposis Coli (hAPC), wherein said transgenic *Drosophila* exhibits abnormal development of dorsal tergites that lack pigmentation, does not reasonably provide enablement for all other transgenic *Drosophila* embraced by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to a transgenic *Drosophila* whose genome comprises the full-length human colon cancer gene Adenomatous Polyposis Coli (hAPC) gene having SEQ ID NO: 1 wherein said transgenic *Drosophila* exhibits developmental abnormalities. The claims are further directed to methods of using the same transgenic

Drosophila to screen for compounds that may inhibit or enhance the phenotypes exhibited said transgenic *Drosophila*.

The specification has taught a transgenic *Drosophila* whose genome comprises a nucleotide sequence encoding full-length hAPC wherein said transgenic *Drosophila* exhibits abnormal development of dorsal tergites that lack pigmentation. However, the specification has not taught other the transgenic *Drosophila* embraced by the claims. In particular, the specification has not provided guidance that correlates expression of hAPC with the full breadth of developmental abnormalities in the context of the claimed transgenic *Drosophila*. Moreover, the working examples provided by the specification fail to support the claim breadth with respect to phenotypes exhibited by claimed transgenic *Drosophila* of all developmental abnormalities as only abnormal development of dorsal tergites that lack pigmentation have been exemplified. Given the lack of guidance provided by the instant specification it would have required undue experimentation to make and use the invention as claimed.

While the specification has provided guidance directed to the creation of a transgenic *Drosophila* whose genome comprises a nucleotide sequence encoding full-length APC, wherein the transgenic *Drosophila* exhibits a phenotype of abnormal development dorsal tergites that lack pigmentation, the specification fails to provide any relevant teachings, guidance, working examples with regard to the production of the other transgenic Drosophila embraced by the claims. One of skill would not be able to rely on the state of the transgenic art for an attempt to produce the other transgenic *Drosophila* broadly encompassed by the claims. This is because the state of the art of

transgenics is not a predictable art with respect to transgene behavior and the resulting phenotype. While the state of the art of transgenics is such that one of skill in the art would be able to produce transgenic *Drosophila* comprising a transgene of interest, it is not predictable if the transgene would be expressed at a level and specificity sufficient to cause a particular phenotype. For instance, the level and specificity of expression of a transgene as well as the resulting phenotype of the transgenic animal are directly dependent on the specific transgene construct. The individual gene of interest, promoter (it is interesting to note that the claims as written do not recite a particular promoter that directs expression of the APC transgene; it is suggested that the claims be amended to include a promoter in operable linkage with the transgene), enhancer, coding, or non-coding sequences present in the transgene construct, the specificity of transgene integration into the genome, for example, are all important factors in controlling the expression of a transgene in the production of transgenic animal which exhibits a resulting phenotype. The claims broadly embrace phenotypes of developmental abnormalities. Given the unpredictability of a phenotype resulting from transgene expression it does that the full scope of developmental abnormalities as recited by the claims is enabled. Moreover, the specification and the state of the art do not support the breadth of the claimed phenotypes directed to developmental abnormalities exhibited by the claimed *Drosophila*. The guidance provided by the instant specification is only correlative to a phenotype of abnormal development dorsal tergites that lack pigmentation. The state of the art as represented by Bhandari et al (Oncogene, 2001, 20: 6871-6880) support the teachings of the instant specification

with respect to the enabled phenotype. In particular Bhandari et al observe in the adult epidermis, of transgenic *Drosophila* expressing full-length APC, the dorsal tergites were not properly developed and were devoid of pigmentation. See page 6873, in column 1 as well as in figure 2, particularly in panel B. As such it appears that the claims as written are overly broad with respect to phenotype and are not supported by the teachings of the instant specification or the art of record. Given the lack of guidance provided by the instant specification and the breadth of the claims directed to all developmental phenotypes it would have required undue experimentation to make and use the invention as claimed.

Therefore, in view of the quantity of experimentation necessary to determine the parameters listed above for the production of transgenic *Drosophila*, the lack of direction or guidance provided by the specification for the production of transgenic hAPC *Drosophila* exhibiting developmental phenotypes other than improper development of dorsal tergites that are not pigmented, the absence of working examples for the demonstration or correlation to the production of a transgenic hAPC Drosophila exhibiting developmental phenotypes other than improper development of dorsal tergites that are not pigmented, the unpredictable state of the art with respect to transgene behavior, and the breadth of the claims drawn all developmental abnormalities, it would have required undue experimentation for one skilled in the art to make and/or use the claimed invention.

Note: Amending the claims to recite a specific phenotype resulting from expression of full-length APC may be sufficient to overcome the instant rejection. Also,

recitation of a particular promoter in operable linkage with the APC transgene is suggested.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4, 10, 12, and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 19 are indefinite as written. The claims are directed to the full-length human colon cancer gene Adenomatous Polyposis Coli (APC) having SEQ ID NO: 1. The specification has not provided a definition of the term full-length gene. It is not clear if the term gene encompasses only a cDNA sequence or if it encompasses the genomic sequence including intron/exon boundaries and promoter etc. As such the metes and bounds of the term full-length gene cannot be determined rendering the claims indefinite. Claims 4, 10 and 12 depend from claim 1. Appropriate correction is required.

Claims 1 and 19 are indefinite as written. The claims are directed to a transgenic Drosophila whose genome comprises the full-length APC gene having SEQ ID NO: 1. The claims are indefinite because SEQ ID NO: 1 is an amino acid sequence and it cannot be determined how a genome (nucleic acid) can comprise an amino acid

sequence. It is well-known that nucleic acid encodes amino acid. Claims 4, 10, and 12 depend from claim 1. Appropriate correction is required.

Claims 1 and 19 recite the limitation "said genomic alteration" in part (a). There is insufficient antecedent basis for this limitation in the claim. Claims 4, 10, and 12 depend from claim 1. Appropriate correction is required.

Claims 1 and 19 provide for the use of the transgenic Drosophila as any assay system, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. Appropriate correction is required. Claims 4, 10 and 12 depend from claim 1.

Claims 1 and 19 are indefinite as written. The claims are indefinite as written because the meaning of the phrase "said genomic alteration allows mis-expression of full-length human APC" is not understood given the lack of definitions provided by the instant specification. In particular, the instant specification has not provided definitions for the terms "genomic alteration" or "mis-expression". As such it not understood what is meant by either term making both the above-recited phrase and the claim indefinite. Appropriate correction is required. Claims 4, 10, and 12 depend from claim 1.

Claim 4 is incomplete as written. The preamble of the claim is directed to a method for selecting a compound for pharmacological activity. The claim is incomplete because the steps of the method do not relate back to the preamble in a positive process. Appropriate correction is required. Claims 10 and 12 depend from claim 4.

Claim 4 recites the limitation "the transgenic fly" in part (a) in line 1. There is insufficient antecedent basis for this limitation in the claim. Claims 10 and 12 depend from claim 4.

Claim 10 is unclear as written. The claim is directed to "a method as claimed in claim 4 wherein, screening and validating efficacy of preventative and therapeutic drugs following APC gene mis-expression". The claim as written is a fragment of a sentence and is confusing, as it does not convey any clear meaning. Appropriate correction is required.

Claim 12 recites the limitation "said drugs" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 12 is unclear as written. The claim is directed to "a method as claimed in claim 4 wherein, concentration of said drugs ranging between 50 to 5000 μg/ml of fly food". The claim as written is a fragment of a sentence and is confusing, as it does not convey any clear meaning. Appropriate correction is required.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is 703-308-8340. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at 703-305-4051. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Official Fax Center number is (703) 872-9306.

Inquiries of a general nature or relating to the status of the application should be directed to Dianiece Jacobs whose telephone number is (703) 305-3388.

Peter Paras, Jr.

Art Unit 1632

PETER PARAS
PATENT EXAMINER